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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/017,788	12/13/2001	Quan Nguyen	002558-064310US	6103

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EXAMINER	
COUNTS, GARY W	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 12/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/017,788	NGUYEN ET AL.	
	Examiner	Art Unit	
	Gary W. Counts	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *October 12, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-60* is/are pending in the application.

4a) Of the above claim(s) *32-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31 and 49-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *10/12/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

The amendment filed October 12, 2004 is acknowledged and has been entered. Claims 49-60 have been added. Claims 1-60 are pending. Claims 32-48 are withdrawn.

Rejections Withdrawn

The objection of claim 3 as failing to further limit the subject matter of a previous claim is withdrawn.

The rejection of claims 1, 18 and 25 as being vague and indefinite is withdrawn in view of the amendments to the claims.

The rejection of claims 1, 3, 5-8, 11, 12 and 15-17 as being anticipated by Tamarkin et al is withdrawn in view of applicant's arguments concerning Tamarkin et al.

Claim Objections

Claim 9 is objected to because of the following informalities: Claim 9, line 2 the recitation "IFN-y.1" should be --IFN-y--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 9 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 9 is vague and indefinite because the claim does not end with a (.) period. Therefore, it is unclear if the claim encompasses other recitations or not.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1, 3, 5-8, 11, 12, 15-17 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al. (US 5,587,294) in view of Barrera et al. (Lymphokine and Cytokine Research, Vol 11, No. 2, 1992, pp. 99-104).

Tamarkin et al disclose a kit comprising a standard diluent and standards (control) to serve as assay standard (col 13). Tamarkin et al disclose that the diluent can be a serum solution (biological fluid) from which endogenous IL-1 or IL2 (target analytes) have been removed (col 16 –col 17). Tamarkin et al disclose known amounts of cytokines are added to the diluent to generate standard curves (col 17, lines 10-44). Tamarkin et al disclose that the kit can contain instructions (col 13, lines 13-16). Tamarkin et al also disclose that the kit comprises a solid phase carrier (support) (col 13). Tamarkin et al disclose that the carrier has immobilized antibodies to capture the target analyte (col 10, lines 44-63) (col 14, lines 21-25). Tamarkin et al also disclose that the solid support can be a bead (microparticles) (col 10, line 64 – col 11, line 6). Tamarkin et al disclose the kit can comprise labeled antibodies for the target analyte (col 14).

Tamarkin et al differ from the instant invention in failing to that the standard diluent is substantially free of two or more different target analytes.

Barrera et al disclose the depletion of cytokines from a biological fluid to be used as diluent in cytokine assays. Barrea et al disclose the removal of two different cytokines from the biological fluid (p. 99). Barrera et al disclose that the removal of these cytokines (target analytes) from the biological fluid provides for a matrix similar to the sample and this avoids loss of paralleism and improves sensitivity.

It would have been obvious to one of ordinary skill in the art to incorporate a diluent that has been depleted of two analytes such as taught by Barrera in the kit of Tamarkin et al because Barrera et al teaches the removal of these cytokines (target analytes) from the biological fluid provides for a matrix similar to the sample and this avoids loss of paralleism and improves sensitivity. Further, this would provide for a single diluent as opposed to two separate diluents and therefore would be more convenient for the test operator.

5. Claims 2, 4, and 50-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al (US 5,587,294) and Barrera et al in view of Van Emon et al (Bioseparation and bioanalytical techniques in environmental monitoring, Journal of Chromatography B, 715 (1998) 211-228).

See above for teachings of Tamarkin et al and Barrera et al.

Tamarkin et al and Barrera et al differ from the instant invention in failing to specifically teach the use of affinity chromatography to remove the two or more different target analytes.

Van Emon et al disclose the use of affinity chromatography to absorb the analyte to be isolated from the sample. Van Emon et al disclose that the analyte is absorbed by its binding partner such as an antibody (p. 213, Bioseparation techniques). Van Emon et al disclose that this provides for methods of successful separation of an analyte of interest from a complex matrix (p. 212).

It would have been obvious to one of ordinary skill in the art to incorporate affinity chromatography such as taught by Van Emon et al for the pre-absorption technique of

Tamarkin et al because Tamarkin et al specifically teaches that the target analytes are removed from the serum by absorption of the target analyte by its respective antibody and Van Emon et al teaches that affinity chromatography provides for methods of successful separation of an analyte of interest from a complex matrix. Therefore, a skilled artisan can have a reasonable expectation of success in incorporating affinity chromatography such as taught by Van Emon et al for the pre-absorption technique of Tamarkin et al.

With respect to the number of different target analytes as recited in the instant claims. The removal of more than two different target analytes is viewed as an optimization of the prior art modified method and kit of Tamarkin et al and Barrera et al wherein two different target analytes are removed from a biological fluid to form a diluent. Absent evidence to the contrary the removal of more than two target analytes and the addition of the more than two analytes to the standard control would merely require adjustment in order to substantially free the biological fluid of the target analytes. Therefore, it would have been obvious to one or ordinary skill in the art to remove more than two different target analytes, since it has long been held that the provision of adjustability, where needed, involves only routine skill in the art. *In re Stevens,* 101 USPQ 284 (CCPA 1954).

6. Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al and Barrera et al in view of Brailly et al (Total Interleukin-6 in Plasma Measured by Immunoassay, Clin. Chem 40/1, 116-123 (1994).

See above for teachings of Tamarkin et al and Barrera et al.

Tamarkin et al and Barrera et al differ from the instant invention in failing to specifically teach the target analytes are two or more of IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, TNF-a and IFN-y.1.

Brailly et al disclose reagents and immunoassays for IL-6. Brailly shows these reagents are specific for IL-6.

It would have been obvious to one of ordinary skill in the art to substitute the reagents of Brailly et al for the IL-1 reagents of Tamarkin et al and Barrera et al because although Tamarkin et al and Barrera et al fails to specifically teach the diluent has had IL-6 removed, Tamarkin et al specifically teaches that their kits and methods can be used to in measuring interleukin-6 (col 7, lines 20-25) (claims 4 and 10) (col 14, lines 33-37) and Barrera et al teaches the removal of analyte for the preparation of a diluent to be used in assays for cytokines. Thus, one skilled in the art would use and package the appropriate reagents for the analyte of interest, in this case interleukin-6.

7. Claims 10, 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al and Barrera et al in view of Posner et al (US 4,994,375).

See above for teachings of Tamarkin et al and Barrera et al.

Tamarkin et al and Barrera et al differ from the instant invention in failing to teach the two or more different target analytes are mixed together to form a single concentrated material.

Posner et al disclose combining different analytes to prepare controls or calibrants (col 2, lines 45-49) (col 3, lines 15-55). Posner et al disclose that the analyte

are mixed and lyophilized and stored for later use (col 3, lines 15-68). Posner et al teaches that this control or calibrant is reconstituted by diluent (col 4).

It would have been obvious to one of ordinary skill in the art to combine the target analytes as taught by Tamarkin et al to form a single concentrated material because Posner et al teaches the combination of different analytes to prepare controls or calibrants which are lyophilized and stored for later use. Further, one of ordinary skill would recognize that the combination of analytes to form a single concentrated material provides for a single control that can replace two or more separate control products.

8. Claims 13, 14, 20-23, 25-28, 30, 31 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al and Barrera et al in view of chandler et al (US 6,268,222).

See above for teachings of Tamarkin et al and Barrera et al.

Tamarkin et al and Barrera et al differ from the instant invention in failing to teach the solid supports are classifiable into subgroups, each subgroup differentiable from others by a differentiation parameter and each subgroup having immobilized thereon a capture reagent capable of bind to a different target analyte.

Chandler et al disclose different populations of microspheres which are classifiable into subgroups. Chandler disclose that the microspheres carry on its surface one or more populations of fluorescently stained nanospheres and that by varying the quantity and ratio of different populations of nanospheres it is possible to establish and distinguish a larger number of discreet populations of carrier particles with unique emission spectra (col 3, lines 1-8). Chandler et al disclose that the unique

emission can be fluorescence (col 12). Chandler et al discloses that each subgroup of the microspheres can be coupled to a different complementary binding moiety (capture reagent) for the analytes of interest (col 15). Chandler et al teaches that these microparticles can be packaged into kits for diagnostic, analytic and industrial applications known in the art (col 4, lines 31-38). Chandler et al teaches that these microspheres provide for a powerful analytical tool, which provides for qualitative and quantitative assay results (col 12, lines 40-42) and provides multiplex analysis of a plurality of analytes in sample (abstract).

It would have been obvious to one of ordinary skill in the art to incorporate microspheres as taught by Chandler et al into the modified kit of Tamarkin et al because Tamarkin et al specifically teaches that the solid support can be beads (microspheres) and Chandler et al shows that such microspheres provide for a powerful analytical tool which provides for qualitative and quantitative assay results and provides multiplex analysis of a plurality of analytes in sample.

9. Claims 24 and 56-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al and Barrera et and Posner et al in view of Van Emon et al (bioseparation and bioanalytial techniques in environmental monitoring, Journal of chromatography B, 715 (1998) 211-228).

See above for teachings of Tamarkin et al, Barrera et al and Posner et al.

Tamarkin et al, Barrera et al and Posner et al differ from the instant invention in failing to specifically teach the use of affinity chromatography to remove the two or more different target analytes.

Van Emon et al disclose the use of affinity chromatography to absorb the analyte to be isolated from the sample. Van Emon et al disclose that the analyte is absorbed by its binding partner such as an antibody (p. 213, Bioseparation techniques). Van Emon et al disclose that this provides for methods of successful separation of an analyte of interest from a complex matrix (p. 212).

It would have been obvious to one of ordinary skill in the art to incorporate affinity chromatography such as taught by Van Emon et al for pre-absorption technique of Tamarkin et al because Tamarkin et al specifically teaches that the target analytes are removed from the serum by absorption of the target analyte by its respective antibody and Van Emon et al teaches that affinity chromatography provides for methods of successful separation of an analyte of interest from a complex matrix. Therefore, a skilled artisan can have a reasonable expectation of success in incorporating affinity chromatography such as taught by Van Emon et al for the pre-absorption technique of Tamarkin et al.

With respect to the number of different target analytes as recited in the instant claims. The removal of more than two different target analytes is viewed as an optimization of the prior art modified method and kit of Tamarkin et al and Barrera et al wherein two different target analytes are removed from a biological fluid to form a diluent. Absent evidence to the contrary the removal of more than two target analytes and the addition of the more than two analytes to the standard control would merely require adjustment in order to substantially free the biological fluid of the target analytes. Therefore, it would have been obvious to one or ordinary skill in the art to remove more

than two different target analytes, since it has long been held that the provision of adjustability, where needed, involves only routine skill in the art. *In re Stevens,* 101 USPQ 284 (CCPA 1954).

10. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Tamarkin et al, Barrera et al and Posner et al.

See above for teachings of Tamarkin et al, Barrera et al and Posner et al.

Tamarkin et al, Barrera et al and Posner et al differ from the instant invention in failing to specifically teach the target analytes are two or more of IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, TNF-a and IFN-y.1.

Brailly et al disclose reagents and immunoassays for IL-6. Brailly shows these reagents are specific for IL-6.

It would have been obvious to one of ordinary skill in the art to substitute the reagents of Brailly et al for the IL-1 reagents of Tamarkin et al and Barrera et al because although Tamarkin et al and Barrera et al fails to specifically teach the diluent has had IL-6 removed, Tamarkin et al specifically teaches that their kits and methods can be used to in measuring interleukin-6 (col 7, lines 20-25) (claims 4 and 10) (col 14, lines 33-37) and Barrera et al teaches the removal of analyte for the preparation of a diluent to be used in assays for cytokines. Thus, one skilled in the art would use and package the appropriate reagents for the analyte of interest, in this case interleukin-6.

Allowable Subject Matter

11. Claims 54 and 60 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

12. The following is a statement of reasons for the indication of allowable subject matter: the prior art of record neither teaches not suggest the eight target analytes are IL-2, IL-4, IL-6, IL-8, IL-10, GM-CSF, TNF-a and IFN-y.

Response to Arguments

13. Applicant's arguments with respect to claims 1-31 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary W. Counts whose telephone number is (571) 2720817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary Counts
Examiner
Art Unit 1641
December 20, 2004

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12/20/04